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Running Title: Benchmark Calculations for Perchlorate

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Abbreviations:
RfD – reference dose
BMD – benchmark dose
BMDL - lower 95% statistical confidence limits on benchmark doses
BMR – benchmark risk
INF – infinite
NOAEL – no adverse effects level
RAIU - radioactive iodine uptake
Tg – thyroglobulin
T3 – triiodothyronine
T4 - total thyroxine
fT4 - free T4
FTI - free T4 index
TSH - thyroid stimulating hormone (TSH)

Abstract

The presence of low concentrations of perchlorate in some drinking water sources has led to concern regarding potential effects upon the thyroid. The National Academy of Sciences recently published a report in which they indicated that the perchlorate dose required to cause hypothyroidism in adults would probably be more than 0.40 mg/kg-day for months or longer. In this paper benchmark doses are calculated for perchlorate from TSH and free T4 serum indicators from two occupational cohorts with long term exposure to perchlorate, and from a clinical study of volunteers exposed to perchlorate for two weeks. The benchmark dose for a particular serum indicator was defined as the dose predicted to cause an additional 5% or 10% of persons to have a serum measurement outside of the normal range. Using the data from the clinical study, the half-life of perchlorate in serum was estimated as 7.5 hours, and the volume of distribution as 0.34 L/kg. Using these estimates, and measurements of perchlorate in serum or urine, doses in the occupational cohorts were estimated and used in benchmark calculations. Because none of the three studies found a significant effect of perchlorate upon TSH or free T4, all of the benchmark dose estimates were indistinguishable from infinity. BMDLs (lower 95% statistical confidence limits on benchmark doses) estimated from a combined analysis of the two occupational studies ranged from 0.21 to 0.56 mg/kg-day for free T4 index and from 0.36 to 0.92 mg/kg-day for TSH. Corresponding estimates from the short term clinical study were within these ranges.